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CONFERENCE ABSTRACTS

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Electro-Acupuncture Improves Insulin Sensitivity in Genetically Obese and Diabetic Mice Through Activation of SIRT1/PGC-1alpha and AMPK in Skeletal Muscle

Fengxia Liang*
*Corresponding Author's Affiliation: Acupuncture & Moxibustion Institute, Acupuncture & Moxibustion and Massage College, Hubei University of Chinese Medicine, Wuhan, China. 315938821@qq.com

Abstract
Aim: Electro-acupuncture (EA) improves insulin resistance in obesity and diabetes, although the biochemical mechanism underlying this effect remains unclear. This study investigated the effect of low-frequency EA on metabolic action in genetically obese and diabetic db/db mice.
Methods: Nine-week-old db/m and db/db mice were randomly divided into four groups: db/m, db/m+EA, db/db, and db/db+EA. Db/m+EA and db/db+EA mice received 3-Hz EA five times/wk for 8 weeks. Fasting blood glucose, body weight, food intake, HbA1c, insulin, and blood lipid levels were measured respectively. Insulin sensitivity was evaluated by intraperitoneal insulin tolerance test (IPITT) and glucose tolerance by intraperitoneal glucose tolerance test (IPGTT). Real-time PCR was employed to assay mRNA expression of genes related to mitochondrial biogenesis and function such as peroxisome proliferator-activated receptorγ (PPARγ) coactivator 1alpha (PGC-1alpha), nuclear respiratory factor 1 (NRF1), and acyl-CoA oxidase (ACOX). Sirtuin 1 (SIRT1) expression, AMP-activated protein kinase (AMPK) activation, and Akt phosphorylation were observed respectively.
Results: EA reduced fasting blood glucose, food intake and body weight while it maintained insulin levels in db/db mice. Improved insulin sensitivity was established in EA-treated db/db mice by IPITT. EA also decreased free fatty acid levels in the db/db mice and increased skeletal muscle SIRT1 protein expression, induced gene expression of PGC-1alpha, NRF1 and ACOX. Furthermore, EA treatment activated AMPK and increased Akt phosphorylation in skeletal muscle of the db/db mice.
Conclusions: EA has a beneficial effect on insulin resistance in obese and diabetic db/db mice, at least partly via stimulating SIRT1/PGC-1alpha and AMPK activity, resulting in improved insulin signal defect.
Keywords: electroacupuncture (EA); diabetes; insulin resistance; SIRT1; obesity

Gender Aspects and Acupuncture

Iréne Lund*
*Corresponding Author's Affiliation: Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. Irene.Lund@ki.se

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Abstract
Pain is one of the most common indications for treatment with acupuncture. The personal experience of pain is a great health problem that is individually varied where both gender and sex related effects likely contribute. Painful experimental stimuli and clinical pain conditions have been described as more intense and partly contributing to limitation of function to a greater extent in women than in men. Women also seem to be overrepresented in many painful clinical conditions such as fibromyalgia, temporomandibular dysfunction, migraine, rheumatoid arthritis and irritable bowel syndrome. The mechanisms underlying the differences between women and men are to a great extent not known but complex interactions between biological, sociocultural and psychological aspects are discussed as is the existence of gender biased research as well as the gap in documentation influencing the knowledge of the differences. The sparse documentation of acupuncture effects related to observed differences between the two sexes are discussed. Preferably, treatment recommendations should be based on studies using both women and men as the norm and the possibly gender related effects have to be further investigated and taken into consideration when designing acupuncture treatment for optimal treatment outcome and rational clinical advices.
Keywords: acupuncture; gender; sex; pain, pain inhibitory systems; knee osteoarthritis

From Bench to Bedside: Translational Studies of Acupuncture for Inflammatory Pain

Lixing Lao*
*Corresponding Author's Affiliation: School of Chinese Medicine, The University of Hong Kong, Hong Kong, China. lxlao1@hku.hk

Abstract
While chronic inflammatory pain, including arthritic pain, causes much physical and emotional suffering, it is often poorly controlled. Anti-inflammatory agents, such as the NSAIDs and Cox-2 inhibitors commonly used to treat inflammatory pain, are associated with adverse effects. Acupuncture has been widely used in China and other Asian countries for thousands of years to treat persistent inflammatory pain and many other conditions. However, it too has limitations in that it might not always be potent enough for severe chronic pain. Our laboratory has been engaged in translational basic science studies with clinical implications to identify synergism between low-dosage morphine, indomethacin, or MK-801 plus acupuncture, and our clinical trial on drug-acupuncture combination therapy demonstrated that this might be the ideal treatment solution for patients with chronic inflammatory pain.
Keywords: acupuncture; inflammatory pain; translational studies; arthritic pain; moarphine; indomethacin

Electroacupuncture in a Rat Model of Early Type 1 Diabetes: Neuroprotective Action through Modulation of Nerve Growth Factor Activity

Manni Luigi*, Soligo Marzia, Protto Virginia
*Corresponding Author's Affiliation: Institute of Translational Pharmacology, National Research Council of Italy (CNR), Rome, Italy. luigi.manni@ift.cnr.it, helen.elden@gu.se

Abstract
Diabetes has been associated with dysfunctions and degeneration of basal forebrain cholinergic neurons (BFCN) that could depend upon defective nerve growth factor (NGF) utilization and incorrect activity-dependent maturation of the precursor ProNGF into mature NGF, with subsequent activation of apoptotic signaling. Electro-acupuncture (EA) could improve brain NGF availability and utilization. We hypothesized that EA could counteract the development of diabetes-associated cholinergic dysfunctions by regulating endogenous brain NGF maturation and utilization.
We used the streptozotocin (STZ) model of type 1 diabetes in young adult rats and assessed the early variations of ProNGF/NGF in the cortex and hippocampus, as well as the features of ProNGF/NGF signaling in the BFCN following STZ and EA at St36.
Four weeks after diabetes induction the ProNGF/NGF ratio was increased in the cortex and hippocampus while the pro-apoptotic c-Jun N-terminal kinase (JNK) signaling, associated with p75NTR receptor activation by ProNGF, was increased in the BFCN. EA counteracted the diabetes-induced deregulation of ProNGF/NGF ratio, de-activated JNK, increased tyrosine kinase-A (TrkA) receptor, Akt and extracellular signal-regulated kinases (ERK) phosphorylation.
Our data, suggesting a possible beneficial effect of EA on brain cholinergic system in diabetes, indicate that the regulation of neurotrophins' expression and activity is one of the possible neurophysiological mechanism underlying acupuncture's effects on brain neurons.

Keywords: diabetic encephalopathy; basal forebrain cholinergic neurons; nerve growth factor; ProNGF; electro-acupuncture; $p75^{NTR}$

Brain Mechanisms Supporting Anti-pruritic Effects of Acupuncture

Vitaly Napadow*, Ang Li, Jieun Kim, Peter Schalock, Ethan Lerner, Bruce Rosen, Ted Kaptchuk, Florian Pfab
*Corresponding Author's Affiliation: Martinos Center for Biomedical Imaging, Massachusetts Gen. Hosp., Charlestown, MA. USA. vitaly@nmr.mgh.harvard.edu

Abstract
Chronic itch is a prevalent symptom of many inflammatory skin disorders, including atopic dermatitis (AD). While conventional systemic approaches to reduce AD itch have shown limited efficacy and/or significant side effects, several recent studies have demonstrated effectiveness of acupuncture for reducing itch in healthy adults and AD. Furthermore, recent evidence suggests that acupuncture effects are partly mediated at the brain level, though specific brain mechanisms underlying acupuncture anti-pruritic effects are currently unknown. We evaluated n = 14 AD patients (age: 25.4 ± 9.1 yrs) showing type-I-sensitivity to grass or birch pollen, cat or dog dander, Dermatophagoides farinae or pteronyssinus. A previously validated itch modulation model was used to create a block design paradigm in conjunction with fMRI (3T, Siemens Trio, Germany). Itch was induced with subject-specific allergen prick testing, and its intensity experimentally increased and decreased using a thermode (Medoc, Israel) alternating between cool (25°C) and warm (32°C) temperature epochs, respectively. Following each scan run, itch was rated using a VAS (0—100). Brain response to itch was investigated before and after real and sham acupuncture. Clinically-relevant allergen itch produced activation in anterior insula (aIns), anterior middle cingulate cortex (aMCC), dorsolateral and ventrolateral frontal gyri, and striatum (putamen, caudate). Real, but not sham, acupuncture was found to reduce itch sensation (ACUP: base = 66 ± 18, post = 44 ± 18, $P < 0.001$; SHAM: base = 57 ± 17, post = 58 ± 22, $P > 0.6$). Following real acupuncture, there was diminished itch-evoked brain activity in right aIns, aMCC, and several striatal areas (putamen, caudate, and nucleus accumbens). There was also less itch-evoked deactivation in a region of S1 contralateral to the acupuncture stimulation. Striatal response to itch may reflect procedural memory and affective/motivational aspects of itch, consistent with the urge to scratch. Down-regulation of brain regions thought to process salience (aIns, aMCC) and affective/motivational (striatum) components of itch in AD, may underlie the efficacy of acupuncture in relieving itch in this clinical population. While much acupuncture research has focused on pain relief, itch has interesting similarities to pain, and more research is needed to explore acupuncture's anti-pruritic effects.
Keywords: itch; putamen; prefrontal cortex; electro-acupuncture; acupoint